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Prior Authorization Review: dalfampridine

Background:
Multiple Sclerosis (MS) is an autoimmune inflammatory demyelinating disease of the central nervous system.[1] Patients with MS may experience cognitive dysfunction, mental and physical fatigue. Dalfampridine (Ampyra®) is a potassium channel blocker used to improving walking in patients with multiple sclerosis.[2] It was approved by the U.S. Food and Drug Administration (FDA) in 2010 to improve mobility in MS patients. The Pharmacy & Therapeutics Committee reviewed this drug previously and approved Prior Authorization (PA) for its use (see **Appendix 1**). The efficacy of dalfampridine to improve walking speed in MS patients was established in clinical trials and confirmed in post-marketing experience. The largest Phase 3 trial compared oral dalfampridine 10 mg twice daily to placebo in 283 adults.[3] The primary outcome was defined as patients who achieved faster walking speeds after 14 weeks of treatment compared to baseline values. The improvement in walking speed was greater in the treatment group compared to placebo (35% vs. 8%, respectively; $p<0.0001$).[3] An open-label extension of the initial Phase 3 trial evaluated long-term safety and efficacy of dalfampridine in 269 patients over 5 years.[4] Throughout the study period mean improvement in walking speed declined but remained improved compared to baseline. Medication related adverse effects were reported in 98.1% of study participants. The most common effects were urinary tract infections, falls, MS relapse, arthralgia and edema. Discontinuation due to adverse effects occurred in 13.8% of patients. Three patients experienced seizures and 3 patients experienced myocardial infarction. No other indications have been approved by the FDA.

The efficacy of dalfampridine has not been established for the treatment of cognitive dysfunction, depression, fatigue or mood swings associated with MS. No other off label uses of oral dalfampridine have been evaluated. Five prior authorization requests were received for dalfampridine in 2015. Three requests were approved and two were denied.

Recommendations:
No changes to the current PA criteria are recommended. No further review or research needed at this time.

References:
1. Harrison DM. Multiple Sclerosis. *Ann Intern Med*. 2014;160(7):ITC4-1. doi:10.7326/0003-4819-160-7-201404010-01004.
2. Ampyra (dalfampridine) [Prescribing Information]. Ardsley, NY: Acorda Therapeutics, Inc., December 2014.
3. Goodman AD, Brown TR, Krupp LB, et al. Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial. *Lancet*. 2009;373(9665):732-738. doi:10.1016/S0140-6736(09)60442-6.
4. Goodman AD, Bethoux F, Brown TR, et al. Long-term safety and efficacy of dalfampridine for walking impairment in patients with multiple sclerosis: Results of open-label extensions of two Phase 3 clinical trials. *Mult Scler*. 2015;21(10):1322-1331. doi:10.1177/1352458514563591.

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Appendix 1: Current Prior Authorization Criteria.

Dalfampridine (Ampyra®)

Goal(s):

- To ensure appropriate drug use and limit to patient populations in which the drug has been shown to be effective and safe.

Length of Authorization:

Up to 12 months

Requires PA:

- Non-preferred drugs

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code	
2. Does the patient have a diagnosis of Multiple Sclerosis?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness
3. Is the medication being prescribed by or in consultation with a neurologist?	**Yes:** Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
4. Is the request for continuation of therapy (patient has completed 2-month trial)?	**Yes:** Go to **Renewal Criteria**	**No:** Go to #5
5. Does the patient have a history of seizures?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #6
6. Does the patient have moderate or severe renal impairment (est. GFR <50 mL/min)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #7

Approval Criteria		
7. Is the patient ambulatory with a walking disability requiring use of a walking aid **OR;** have moderate ambulatory dysfunction and does not require a walking aid AND able to complete the baseline timed 25-foot walk test between 8 and 45 seconds?	**Yes:** Approve initial fill for 2-month trial.	**No:** Pass to RPh. Deny; medical appropriateness

Renewal Criteria		
1. Has the patient been taking dalfampridine for ≥2 months with documented improvement in walking speed while on dalfampridine (≥20% improvement in timed 25-foot walk test)?	**Yes:** Go to #2	**No:** Pass to RPh. Deny; medical appropriateness
2. Is the medication being prescribed by or in consultation with a neurologist?	**Yes:** Approve for 12 months	**No:** Pass to RPh. Deny; medical appropriateness

Clinical Notes:

- Because fewer than 50% of MS patients respond to therapy and therapy has risks, a trial of therapy should be used prior to beginning ongoing therapy.
- The patient should be evaluated prior to therapy and then 4 weeks to determine whether objective improvements which justify continued therapy are present (i.e. at least a 20% improvement from baseline in timed walking speed).
- Dalfampridine is contraindicated in patients with moderate to severe renal impairment.
- Dalfampridine can increase the risk of seizures; caution should be exercised when using concomitant drug therapies known to lower the seizure threshold.